Non-technical Abstract

In the United States, over 50,000 patients per year develop colon cancer that has spread to the liver (Meta-analysis Group, 1998). Surgery offers patients with liver cancer a one-third chance of cure, but patients with tumors that cannot be surgically removed have few effective treatment options (Fong et al., 1995). The average time to disease progression is 6 to 9 months in these patients, while overall survival is 12 to 18 months (O'Connell et al., 1998).

MediGene, Inc. is currently studying a tumor-killing virus, NV1020, as a potential new treatment for patients with colorectal cancer that has spread to the liver. NV1020, the virus used in this study, is a weakened version of the herpes virus that causes cold sores (called herpes simplex virus type 1 or HSV-1). NV1020 was extensively tested in HSV-sensitive animal models before it was administered to people in clinical studies.

MediGene, Inc. is testing the safety and anti-tumor effectiveness of NV1020 in an ongoing clinical study (identified as protocol NR1-001) in study volunteers with colon cancer that has spread to the liver. Only people who have antibodies to HSV-1 have been enrolled in study NR1-001. To date, 10 study volunteers have received NV1020 without experiencing any serious NV1020-related side effects. The study is continuing to enroll.

MediGene, Inc. would like to continue to study NV1020 as a potential therapy for patients with colon cancer that has spread to the liver. The new study (identified as protocol NR1-003) is designed to test the safety and anti-tumor effectiveness of NV1020 in study volunteers who do not already have antibodies against HSV-1. People who volunteer for this study and are enrolled will have a CT scan and a physical exam before receiving a single injection of NV1020 into a blood vessel that leads directly into the liver. During this injection both the right and left groin will have a tube threaded inside; one tube will be used to infuse the NV1020 and the other tube will be used to draw off small blood specimens at frequent intervals in order to learn about how NV1020 moves through the liver. The first group of three study volunteers will receive a dose of NV1 020 that was already tested in protocol NR1-001, and was found to be safe. If this initial dose is safe in these study volunteers who do not have antibodies to HSV-1, then higher doses of NV1020 will be tested in three sequential groups consisting of three study volunteers each until a maximum tolerated dose is reached. An optional increase to a fifth dose may be considered. Three to 10 days after the injection of NV1020, study volunteers may undergo an operation for the placement of an infusion pump. This pump is connected to a tube that threads into a blood vessel that leads directly into the liver. The liver pump may be used to administer chemotherapy at study centers where that kind of treatment is available. At the time of the operation to place the liver pump, two small pieces of liver tumor as well as two small pieces of normal liver tissue will be

collected to see if they contain NV1020. If putting a pump in is not thought to be best for the patient, or if liver pumps are not used for chemotherapy at a particular study center, the same liver tumor and normal tissue samples will be collected using a picture-guided needle biopsy. In keeping with the procedure used to sample liver tissue during the pump placement operation, a maximum of four liver sites will be sampled. Study volunteers will be closely monitored throughout the study, and medical tests will be performed at specific study time-points to assess the safety and anti-tumor effectiveness of NV1020. After 3 months, study volunteers will be followed in a long-term study (identified as NR1-004).

References

Fong et al. *CA Cancer J Clin* **45**: 50-62 (1995)

Meta-Analysis Group in Cancer *J Clin Oncol* **16**:301-308 (1998)

O'Connell et al. *J Clin Oncol* **16**:2528-2533 (1998)